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BAY 11-7082, an anti-inflammatory drug attenuates metastasis potential of Pak1 over expressing cells by modulating Pak1-NF- κ B-p65-fibronectin signaling network

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P₂₁-activated kinase 1 (Pak1) - a serine/threonine kinase, is a well-known regulator of cytoskeletal remodelling, cell motility, cell proliferation, and cell survival, which can induce phosphorylation and activation of NF- κ B, that can accelerate growth and survival of cells. Our previous study have implicated that Pak1 by itself can have an oncogenic role in pancreatic cancer through Pak1-NF-kappaB-p65-fibronectin pathway. Hence agents blocking downstream target of Pak1, namely NF- κ B and its activation, may reduce the invasiveness of pancreatic cancer. To test this hypothesis, we used BAY 11-7082 a known NF- κ B inhibitor and an anti inflammatory drug for the study. In the present study, we found BAY 11-7082 inhibited migration and invasive capability of Pak1 over expressing pancreatic cell lines through blocking p65 NF- κ B- Fibronectin pathway. We also observed reduced fibronectin promoter activity on BAY 11-7082 treatment. Thus, the inactivation of NF- κ B pathway, down-regulated fibronectin expression and reduces the metastasis potential of Pak1 over expressing pancreatic cancer, indicating targeting Pak1-NF-kappaB-p65-fibronectin pathway might be an efficient treatment modality for pancreatic cancer patients.

Biography

SankarJagadeeshan is a graduate in Biotechnology, Chemistry and Zoology from University of Kerala and a post graduate in Biotechnology from Vellore Institute of Technology, VIT University, Tamil Nadu. He has seven years of research experience in molecular oncology, translational biology, nanomedicine and drug delivery as well as identification of novel drugs for cancer therapy. He had worked in premier institute of India viz., Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram, Kerala and Indian Institute of Technology Madras, Tamil Nadu as research fellow. He has published nine papers in the field of microbiology, medicinal chemistry and oncology and has two book chapters to his account. Currently he is a research scholar in Department of Genetics in University of Madras working on the role of p21 activated kinase 1 in progression, metastasis, drug resistance and angiogenesis during pancreatic carcinogenesis.

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